# THE CHEMICAL AFFINITY OF MUCUS FOR HYDROCHLORIC ACID.[1]

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SOME months ago, with the co-operation of Dr. A. V. S. Lambert, I began a study of the secretion of HCl under various conditions. Dogs were used, and the gastric juice was obtained by means of Pawlow fistulæ. In the course of the experiments it was noted that while the gastric juice collected from the artificial stomach had no opportunity to come in contact with the food, yet a considerable fraction of the HCl always existed as combined acid, whereas all the acid apparently should have been uncombined free acid. At first this result was supposed to be due to some serum which had run into the collecting funnel from the stitch margin of the fistula along with the gastric juice; but a month later, when the wound was healed, this explanation did not appear adequate. It had also been noted that the mucus in the collecting receptacle varied from hour to hour, and that when the amount of mucus was considerable the combined acid was also increased.

In his studies of the secretion of acid in the stomach Pawlow observed a fluctuation which he thought might be explained by different rates of flow—that is, when the gastric juice was rapidly secreted it passed quickly over the mucous membrane and was not so much "neutralized" as when the secretion was slow. Pawlow speaks of the mucous membrane as "alkaline." I am unable to determine from his papers whether Pawlow determined the total amount of HCl in the gastric juice as well as the free acid, but I am led to think he did not, because of his conclusion that the amount of HCl secreted in the stomach during the digestive period is constant. I am unable to find any reference in the papers of Pawlow or his pupils relative to mucus as a "neutralizing" medium for HCl in the stomach.

The function and fate of the mucous secretions in the various parts of the gastrointestinal canal are relatively unknown, in a physiological as well as a chemical sense. In the stomach mucus is constantly being secreted to some extent, but more at some times than at others, as, for example, at the end of a digestive period; and in certain pathological conditions the amount of this secretion is quite considerable.

Several years ago it was observed in this laboratory that "precipitated mucoid shows practically no combining power with acids. In the hydration of mucoid by pepsin acid, however, acid combines

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[1] Received for publication September 30, 1906.

with the dissolved protein products formed in the process."[2] It seemed probable that similar behavior of the gastric mucus accounted for the constant occurrence of combined acid in the juice obtained, and at Gies' suggestion the following experiments were conducted along lines similar to those that had been performed on mucoid.

Mucus from pigs' stomachs was used.[3] In the first series of determinations this mucus was dissolved in 0.5 per cent. $Na_2CO_3$. The solution was filtered, neutralized with dilute HCl, and precipitated by means of alcohol. This precipitate was collected on a filter and washed with water. Mucous protein obtained in this way is only slightly soluble in water and is neutral in reaction.[4] A suspension in water was made of this mucous product, and to it was added $^{3n}$ HCl until the solution gave just a faint reaction for free acid with Günsberg's reagent. Under these conditions, while there is some combining affinity of mucous protein for HCl, it is insignificant.

On the other hand, when 0.1 gram of pepsin[5] is added to such a mucous suspension the result is marked, as shown in the following summary of data obtained in one of the experiments:

### TABLE I.

Aqueous suspension of about 1 gram of dry mucous protein and 0.1 gram pepsin. Titration with $\frac{3}{20}$ normal HCl.

1.4 c.c. produced reaction for combined acid.

1.6 c.c. produced faint reaction with Günsberg's reagent.

1. After digesting 24 hours in a thermostat at 40° C. there was no free acid present. 2.7 c.c. $_{3n}$ HCl added.
2. After digesting 48 hours.[6] No free acid present. 0.5 c.c. $\frac{3n}{20}$ HCl added.
3. After digesting 72 hours. Free acid present.
4. After digesting 96 hours. No free acid present. 2.5 c.c. $\frac{3n}{20}$ HCl added.
5. After digesting 120 hours. Free acid present.
6. After digesting 144 hours. No free acid present. 2 c.c. $\frac{3n}{20}$ HCl added.
7. After digesting 168 hours. No free acid present. 2 c.c. $\frac{3n}{20}$ HCl added.
8. After digesting 192 hours. Free acid present and persistent.

Total acid added 11.3 c.c.

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[2] Gies, Proceedings of the American Physiological Society, p. xiii; Amer. Jour. of Physiol., viii, 1903. Also Gies and collaborators, Biochemical Researches, 1903, i, p. 54.

[3] It was obtained mechanically by lightly scraping the surface of the mucous membrane.

[4] The relation of this result to the studies of salts of mucoids, nucleoproteins, etc., now in progress in this laboratory, will be pointed out later.

[5] Parke, Davis & Co., 1 to 2000.

[6] All records of time in these summaries designate *total* periods from the beginning of digestion.

### TABLE II.

Control conditions same as in Table I. 2 c.c. $\frac{3n}{20}$ HCl added.
1. After digesting 24 hours. No free HCl. 2 c.c. $\frac{3n}{20}$ HCl added.
2. After digesting 48 hours. No free HCl. 2 c.c. $\frac{3n}{20}$ HCl added.
3. After digesting 72 hours. No free HCl. 4 c.c. $\frac{3n}{20}$ HCl added.
4. After digesting 96 hours. Free acid present.
Total acid added 10 c.c.

The mucus-hydrochloric acid mixtures in these two experiments were combined, and, when filtered and after being neutralized, were submitted to tests for the products of digestion. These digestive products consist almost wholly of proteoses, with only a trace of peptones.

A second series of observations was made in which, instead of the precipitated mucous protein used in the previous experiments, I employed the fresh mucus as it is immediately after its removal from the pig's stomach. The observations were not intended to be strictly quantitative, but they served well the chief purpose in view, that is, to ascertain whether fresh mucus combines with acid. The mixtures were kept well covered with toluol and the digestion carried on at a temperature of 40° C. The results were as follows:

### FLASK I.

Mucus, 2 grams; water, 25 c.c.
Pepsin, 50 mg.; $^{3n}$ HCl, 4 c.c.
1. 24 hours. Free acid present.
2. 48 hours. No free acid present. 2 c.c. $\frac{3n}{20}$ HCl added.
3. 72 hours. Doubtful reaction. 1 c.c. $\frac{3n}{20}$ HCl added.
4. 96 hours. Free acid present.
5. 120 hours. Free acid present.
6. 144 hours. Free acid present.
Total acid added 7 c c.

### FLASK II.

Mucus, 2 grams; water, 25 c.c.
Pepsin 100 mg.; $\frac{3n}{20}$ HCl, 4 c.c.
1. 24 hours. No free acid. 2 c.c. $\frac{3n}{20}$ HCl added.
2. 48 hours. No free acid. 2 c.c. $\frac{3n}{20}$ HCl added.
3. 72 hours. Free acid present.
4. 96 hours. No free acid present. 2 c.c. $\frac{3n}{20}$ HCl added.
5. 120 hours. Free acid present.
6. 144 hours. Free acid present.
Total acid added 10 c.c.

### FLASK III.

Mucus, 2 grams; water, 25 c.c.
Pepsin, 200 mg.; $\frac{3n}{10}$ HCl, 2 c.c.
1. 24 hours. No free acid 4 c.c. $\frac{3n}{10}$ HCl added.
2. 48 hours. Free acid present.
3. 72 hours. Free acid present.
4. 96 hours. No free acid. 2 c.c. $\frac{3n}{10}$ HCl added.
5. 120 hours. Free acid present.
6. 144 hours. Free acid present.
Total acid added 8 c.c.

### FLASK IV.

Pepsin, 100 mg.; water, 25 c.c.; $\frac{3n}{10}$ HCl, 4 c.c. No mucus.
1. 24 hours. Strong reaction for free acid.
2. 48 hours. Strong reaction for free acid.
3. 72 hours. Strong reaction for free acid.
4. 96 hours. Strong reaction for free acid.
5. 120 hours. Strong reaction for free acid.
6. 144 hours. Strong reaction for free acid.

The pepsin-acid solution was titrated against $\frac{3n}{10}$ NaOH in the last case, 3 c.c. being required to neutralize the free HCl present. The 1 c.c. which had been found was probably in combination with some proteid material such as proteose that existed as impurity in the pepsin preparation.

It is clear, I think, from these results, that mucus, like albumin and other proteins, is capable, in the presence of pepsin, of combining with hydrochloric acid. This is true not in a slight degree, but to a relatively marked extent. It is probable, also, it seems to me, that in the stomach the combining power of fresh mucus, as it is secreted from the gland, is much greater than these experiments indicate, because in using, as I have had to do, mucus removed from the stomachs of pigs that had probably not been recently fed, a hunger stimulus would have excited the flow of some gastric juice, and thus would largely have satisfied the combining power of the mucus used in the experiments.

However that may be, the combining power of mucus with HCl, as demonstrated in these experiments, is sufficient to explain some of the physiological and pathological phenomena that are well recognized. For example, in certain morbid gastric conditions there is observed a marked diminution in the amount of free HCl, while the total acidity (exclusive of organic acids) is often almost or quite normal. Along with this there is an excessive secretion of mucus. In such states it does not seem unlikely that the combined acid is bound with mucus, and the condition resembles that observed in dogs with Pawlow fistulæ, in that during the later periods of digestion mucus is secreted abundantly, and often at such times there is only a trace of free HCl, while the total acidity may be considerable.